

5,047,335 (hereafter, Paulson et al.) in view of Weitzhandler et al., (1994) J. Pharm. Sciences 83(12)1670-1675 (hereafter, Weitzhandler et al.) and "art disclosed in the specification (page 16)." (Paper 10, page 2). Applicants respectfully traverse.

The Office contends that Paulson et al. describe methods of producing proteins with a particular glycosylation pattern and that such proteins are useful for research and diagnostic purposes. The Office states that Weitzhandler et al., describe that treatment of a particular oligosaccharide structure (structure 1 of Figure 2 of Weitzhandler et al.) sequentially with peptide N-glycosidase F (PNGase F) and a Jack bean enzyme would result in a G-2 oligosaccharide. (Paper 10, page 3). Further, the Office contends that Applicants have disclosed a variety of therapeutically useful anti-CD20 antibodies (Paper 10, page 3). The office has asserted that in view of these disclosures, it would have been prima facie obvious to one of ordinary skill in the art at the time the present invention was made to have created the claimed inventions. (Paper 10, page 3). The Office contends that in view of Paulson et al. and Weitzhandler et al., the skilled artisan would have been motivated to create altered versions of therapeutically useful antibodies such as anit-CD20 antibodies in order to assess the role of oligosaccharide function in the therapeutic effect seen when the antibody was administered. (Paper 10, page 3). Applicants submit that the Office has failed to make out a case for prima facie obvious of claims 1-16, 36, 38, 42 and 44.

It is well settled that in order for the Office to establish a prima facie case of obviousness the office must establish that the prior art relied upon, coupled with knowledge generally available in the art at the time of the invention, contains some

suggestion or incentive that would have motivated the skilled artisan to modify a reference or to combine a number of references to arrive at the claimed invention. However, none of the references relied upon by the Office describe or suggest the claimed composition and their disclosure does not support that they can be modified or combined in any manner to result in the claimed invention. As acknowledged by the Office, Paulson et al. do not describe or suggest a glycoprotein composition such as the one claimed. (Paper 10, page 3). Further, while Weitzhandler suggest that the expected result of the treatment of a particular oligosaccharide structure with PNGase F and a Jack bean enzyme would be another structure (FucMan3GlcNAc2), Weitzhandler does not describe or suggest a composition such as the composition of claim 10 substantially free of CH2 domain containing other oligosaccharides. Figure 7 referred to by Weitzhandler to describe the oligosaccharide structures in the composition resulting from the chemical digestion of a polyclonal antibody with PNGase F and Jack bean enzyme makes it evident that the procedure performed on a polyclonal composition results in a glycoprotein compositions having a number of different oligosaccharide structures. While the two enzymes modify one of the structures present, they do not result in a composition which is substantially free of other oligosaccharide structures (see the results of enzymatic digestion in Figure 7B, page 1675). Therefore, neither of the primary references disclose or suggest the claimed compositions. Further, neither the Office nor the references themselves suggest any modifications to result in the claimed invention. Finally, the combination, assuming arguendo that some suggestion to combine the references in the manner suggested by the office exists, would not result in the claimed invention nor provide any suggestion that such a result could be

achieved. A cell type transfected with a glycosyltransferase as disclosed by Paulson et al. would not be expected to produce a composition substantially free of certain other oligosaccharide structures alone or in combination with the Weitzhandler enzyme treatment. Any discussion relating to particular antiCD20 antibodies in the specification is moot in view of the foregoing.

In view of the foregoing Applicants respectfully suggest that the Office has failed to make out a case for unpatentability of the claimed invention under 35 U.S.C. § 103(a) and Applicants respectfully request withdrawal of the pending rejection of the claims on this basis.

CONCLUSION

Applicant respectfully requests that the foregoing remarks be considered and entered in the file history of the above-identified application. It is submitted that all grounds for rejection have been removed and the claims are now in condition for allowance. It is therefore earnestly solicited that such a final favorable disposition is made. The Examiner is invited to telephone Jeffrey S. Kubinec, Esq. (Reg. No. 36,575) at (650) 225-8228 if deemed helpful to clarify and advance prosecution.

Respectfully submitted,
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